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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,226	04/30/2001	Gerald Koelsch	2932.1008-003	4183

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 08/08/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,226	KOELSCH ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2001 and 10 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

ACKNOWLEDGMENT OF PRELIMINARY AMENDMENT, SEQUENCE LISTING, IDS, STATUS OF THE APPLICATION AND CLAIMS

1. The preliminary amendment, the Information Disclosure Statements (IDS) and Form PTO-1449 filed 4/30/01 and 2/10/03, respectively are acknowledged, entered and considered. This is a divisional of co-pending U.S. application Serial No. 09/603,713, filed 6/27/00, which claims the benefit of U.S. provisional applications Serial Nos. 60/141,363, 60/168,060, 60/177,836, 60/178,368, and 60/210,292, filed 16/28/99, 11/30/99, 1/25/00, 1/27/00, and 6/8/00, respectively. In view of Applicant's request, the computer-readable form of the sequence listing of the parent application Serial No. 09/603,713, filed 6/27/00 has been transferred to the instant application Serial No. 09/845,226, filed 4/30/01 since the computer-readable form of the sequence listing of this application is identical to that in the parent application 09/603,713. Thus, in accordance with 37 C.F.R. 1.821(e), the computer-readable form of the sequence listing filed in the parent application has been entered and considered in the instant application.

In regard to IDS filed 2/10/03 (Paper No. 11), in view of Applicant's request, the references cited therewith in Form PTO-1449 are not provided in the instant specification. However, as per Applicant's request, since some of the cited references were considered previously in the parent application Serial No. 09/603,713, pursuant to 37 CFR § 1.98(d), some of the references cited in Form PTO-1449 in this application have been considered and signed as requested by Applicant. Nevertheless, the IDS

and Form PTO-1449, filed 4/30/01 (Paper No. 3) are not considered and signed as requested by Applicant because the references cited therewith are not with the instant application or with the parent application. The references cited in the IDS filed 4/30/01 (Paper N0. 3) should be provided, except for a reference, which is identified with an asterisk (*), which is enclosed and initialed and signed by the Examiner. In view of Applicant's request, claims 1-20 have been canceled and claims 24-26 have been added. Thus, claims 21-26 are now pending in the application.

OBJECTION TO TRADEMARK AND ITS USE

2. The use of the trademark "FPLC RESOURCE-Q™" has been noted in this application. Although, the use of trademark is permissible in patent applications, the proprietary nature of the mark should be respected and every effort made to prevent its use in a manner, which might adversely affect its validity as trademark. Further, the specification, which specifies the generic terminology should include, published product information sufficient to show that the generic terminology or the generic description is inherent in the article referred by the trademark. This description requirement is made because the nature and composition of article denoted by trademark can change and affect the adequacy of the disclosure.

CLAIMS REJECTION-35 U.S.C. 112 1st PARAGRAPH.

3. Claims 21-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of memapsin 2 by OM99-1 and OM99-2 inhibitors and use of said inhibitors in designing, synthesizing and testing of inhibitory

activity toward the enzyme *in vitro*, does not reasonably provide enablement for a method for treating a patient to decrease the likelihood of developing or progressing of Alzheimer's disease by administering to the individual an effective amount of memapsin 2 in the manner claimed in claims 21-23, and to a method of modeling using a computer program based on the crystallization of memapsin 2 or based on the parameters for memapsin shown in Table 2 as claimed in claims 24-26. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not adequately teach employing a computer program useful in treatment and/or prevention of Alzheimer's disease as presently claimed in claims 21-26; rather, the specification teaches the use of memapsin 2 in a method of cloning (Example 1), distribution (Example 2), expression, refolding and purification (Example 3), proteolytic activity (Example 4), activation (Example 5), Expression in mammalian cells (Example 6), design and synthesis (Example 7), and measurement of enzymatic activity *in vitro* (Example 8).

Therefore, the instant specification does not commensurate with the claimed subject matter in which the compound used as an effective inhibitor of memapsin 2 is expected to be particularly useful in the treatment and/or prevention of Alzheimer's disease. Thus, there is no evidence or data to show that a similar regimen can be used for treating a patient to decrease the likelihood of developing or the progression of Alzheimer's disease by administering to the individual an effective amount of an inhibitor

of memapsin 2 having an K_i of less than or equal to 10^{-7} M or which binds to crystallized enzyme characterized by the parameters in Table 2 when bound to OM99-2.

Thus, in view of the above, and in view of the fact that there is no enablement in the instant specification for the method of treating and/or preventing of Alzheimer's disease by administering an effective amount of an inhibitor of memapsin 2 compound claimed, and further in view of the complexity of Applicant's invention and the state of the art of treating and/or preventing of Alzheimer's disease, with the compound claimed; the Examiner is unable to determine the enablement of the invention as claimed without appropriate evidence or data. Such evidence in the art of treating cognitive dysfunctions details the state of the art in this area and establishes that even the disease is very hard to diagnose, let alone to treat and/or prevent. For example, Ezzell (Scientific America, pages 152-153, March 7, 1993) states on page 152, middle column, before last paragraph that doctors can only diagnose Alzheimer's through a process of elimination, ruling out other disorders such as a slight stroke, a brain tumor, or even an adverse drug reaction. A definitive diagnosis must await death and autopsy, when a pathologist can view the telltale "senile plaques" that pock the brains of Alzheimer's victim. Further, Varon et al. (Dev. Neurosci., Vol. 6, pp. 73-100, 1983/1984) discuss the implications of neurotrophic and neurite-promoting factor and their clinical potential in neuronal diseases such as Parkinson, ALS and Alzheimer in which the authors concluded by stating that further clinical progress requires a better understanding of neurobiological bases of nerve regeneration. Furthermore, Cordell et al. (U.S. Patent No. 5,221,607) discuss that the etiology of Alzheimer's disease is unknown and up to

date, there are no means available to treat the pathogenesis of Alzheimer's disease and the paucity of understanding concerning the mechanism of amyloid formation in Alzheimer's disease is a major obstacle in the development and design of therapeutic agents that can intervene in this process (See e.g., Col.1, lines 55-67). Similarly, Nelson et al. (U.S. Patent No. 5,252,463) discuss serious diseases affecting the central nervous system, which referred as neuropathologies such as Alzheimer's disease and Down's syndrome in which the etiology of Alzheimer's disease is unknown (See e.g., column 1). Thus, the prior art clearly show the unpredictable nature and the complexity of the art in regard to treatment and/or prevention of Alzheimer's disease. Therefore, considering the nature of the treatment and/or prevention of Alzheimer's disease by administering an effective amount of inhibitor of memapsin 2 claimed and the limited success achieved; one skilled in the art would not accept the instantly claimed invention as obviously valid and correct without demonstration of evidence or data for the following reasons:

In view of the fact that animals and humans are out bred, in view of the lack of disclosure of suitable animal models for a method of treating or preventing cell death in the central or peripheral nervous system, in view of the recognized problems in the art regarding effective treatment of diseases affecting the nervous systems (neuropathologies) and in view of the fact that it is difficult to regenerate the neurons in the living body; a reasonable doubt exists as to the enablement of the claimed method of treating and/or preventing Alzheimer's disease in a subject and particularly in a human by administering an effective amount of inhibitor of memapsin 2 claimed. Thus,

the claims are based on pure speculation that the method would be effective since Applicant has not established any *nexus* between an effective amount of the claimed inhibitor of memapsin 2 and its use in the manner claimed.

Further, the first paragraph of 35 U.S.C. 112 requires, *inter alia*, that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not directed to disclose every species that falls within a generic claim, id. At 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, in view of the above, and in view of the fact that there is no enablement in the instant specification for treating and/or preventing Alzheimer's disease by administering an effective amount of inhibitor of memapsin 2. Thus, applying the *Wands* factors to the facts of this case, one of skill in the art would find that

undue amount of experimentation would be required to practice the full scope of the extremely broad claims fro the reasons given above. Hence, in view of the quantity of experimentation necessary, the lack of adequate guidance or working examples or data, and the breadth of the claims, the claims are not commensurate in scope with the enabling disclosure. Accordingly, filing of evidence commensurate with the scope of the claims or amendment of the claims to what is supported by the enabling disclosure is suggested.

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 21-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21 and 25-26 are indefinite and confusing in referring back to parameters in Table 2 in the specification because referring back to a Table or a Figure or a Number is not acceptable claim language. Such material should be incorporated within the claim language. Further, it is long standing Office practice that claims should be completed and self-contained and incorporation into claims by express reference to the specification is not permitted and should not be relied on to define the invention (*Ex parte Fressola*, Bd. Pat. Appl. & Inter., 5/11/93, p. 1608).

Claim 23 is indefinite in the recitation the acronym "APP". Use of the full terminology at least in the first occurrence would obviate this rejection.

CONCLUSION AND FUTURE CORRESPONDENCE

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The appropriate fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
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AAM Mohamed/AAM

August 5, 2003